Incidence of Childhood Type 1 Diabetes Worldwide

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CEJECTVE— To investigate and monitor the patterns in incidence of childhood type 1 diabetes worldwide.

RESEARCH DESIGN AND INETHODS— The incidence of type 1 diabetes (per 100,000 per year) from 1990 to 1994 was determined in children ≤14 years of age from 100 centers in 50 countries. A total of 19,164 cases were diagnosed in study populations totaling 75.1 million children. The annual incidence rates were calculated per 100,000 population.

RESULTS— The overall age-adjusted incidence of type 1 diabetes varied from 0.1/100,000 per year in China and Venezuela to 36.8/100,000 per year in Sardinia and 36.5/100,000 per year in Finland. This represents a >350-fold variation in the incidence among the 100 populations worldwide. The global pattern of variation in incidence was evaluated by arbitrarily grouping the populations with a very low (<1/100,000 per year), a low (1/4.99/100,000 per year), an intermediate (5-9.99/100,000 per year), a high (10-19.99/100,000 per year), and a very high (10-19.99/100,000 per year) incidence. Of the European populations, 18 of 39 had an intermediate incidence, and the remainder had a high or very high incidence. A very high incidence (100,000 per year) was found in Sardinia, Finland, Sweden, Norway, Portugal, the U.K., Canada, and New Zealand. The lowest incidence (1/100,000 per year) was found in the populations from China and South America. In most populations, the incidence increased with age and was the highest among children 10-14 years of age.

CONCLUSIONS— The range of global variation in the incidence of childhood type 1 diabetes is even larger than previously described. The earlier reported polar-equatorial gradient in the incidence does not seem to be as strong as previously assumed, but the variation seems to follow ethnic and racial distribution in the world population.

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he global variation in the incidence of type 1 diabetes among children ≤14 years of age has been confirmed to be large (1–5). Among Caucasoid populations, the incidence is higher than among Mongoloids and Negroids, although significant geographic differences are evident in inci-

dence within each major ethnic group (2,4–12). Large differences in incidence have been reported in Caucasoid populations living in relatively close proximity and among those who are genetically similar. For example, the incidence in the Nordic countries (Finland, Sweden, and Norway) is 2–4

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Abbreviations: DiaMond, Diabetes Mondiale; WHO, World Health Organization.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

times higher than that in Estonia (3,4, 13,14) and 2-3 times higher than that in Iceland (15). Large interethnic differences in the incidence rates between Jewish and Arab populations have been reported in Israel (16). Geographical variation in incidence appears to reflect the global distribution of major ethnic populations, which demonstrates a different degree of genetic susceptibility to diabetes among populations. Although genetic susceptibility is necessary for the development of type 1 diabetes, the etiology of this disease is a multifactorial one. The wide global variation in incidence between and within major ethnic groups suggests that environmental factors are significant in the etiology of type 1 diabetes. Unfortunately, our knowledge about the possible environmental risk factors for type 1 diabetes is still very limited.

Most of the information regarding type 1 diabetes incidence thus far has come from regions with a high or intermediate incidence, mostly in Europe and North America where several registries have been established since the mid-1980s or earlier. The data from Asia, South America, and Africa are still sparse. Setting up and maintaining population-based registries in verylow-incidence areas such as South America, Asia, and Africa are extremely difficult. The lower the incidence, the larger the surveillance population must be to obtain stable estimates for rates. However, the availability of reliable standardized data on type 1 diabetes incidence from these low incidence areas is particularly important to confirm that the presumed large variation in incidence exists and that a low incidence in those areas is true and is not a result of an underestimation of the incident cases.

Because of the dearth of information available and limited research into the public health implications of type 1 diabetes, the World Health Organization (WHO) began the Multinational Project for Childhood Diabetes (DiaMond) in 1990 (17). One of the main objectives of this effort is to investigate and monitor the patterns in incidence of type 1 diabetes in children up to the year 2000. In addition, substudies assess the genetic risk factors associated with the disease to study mortality and complications in type 1 diabetes, to evaluate health

care and health economics associated with diabetes, and to promote training programs in diabetes epidemiology research.

The primary goal and the initial aim of the WHO DiaMond project is the surveillance of the incidence of type 1 diabetes among children ≤14 years of age worldwide. Population-based registries are used to collect standardized data on incidence (17). The accomplishment of this goal depends on close cooperation among the participating centers and a standardized approach to data collection and reporting. Standardized incidence data on type 1 diabetes have been collected for the WHO DiaMond project since the year 1990. Herein, we report the age- and sex-specific incidence from 1990 to 1994 worldwide.

RESEARCH DESIGN AND IVETHOOS

Organizational structure of the WHO DiaMond incidence study

The WHO DiaMond Incidence Data Center located at the Diabetes and Genetic Epidemiology Unit of the National Public Health Institute in Helsinki, Finland, has served as the coordinating center for the DiaMond incidence study. Two DiaMond coordinating centers (in Helsinki, Finland, and Pittsburgh, PA) together developed the standards for the incidence studies, assisted in processing the data, and assisted in the coordination of the data analysis. Each of the 100 participating centers is headed by a local principal investigator who was responsible for data collection and for the day-today aspects of the fieldwork (see APPENDIX). To be eligible to participate in the WHO DiaMond study, each center must have a well-defined population-based registry where the incidence is accurately defined. Every participating center prepared its own local methods of operation for the incidence study by following the framework provided by the WHO DiaMond incidence study. In the local methods of operation, centers described the population base, the design of the registry, sources of data, data management, data items, and the time schedule for data collection.

Incidence study population

The denominator for the analysis was children ≤ 14 years of age with residency in the study area, which was defined geographically to correspond with administrative and census boundaries. The total number of people ≤ 14 years of age in the

populations collaborating in the WHO DiaMond incidence study is 75.1 million. The numerator comprises 19,164 children ≤14 years of age diagnosed with type 1 diabetes from 1990 to 1994 in the WHO DiaMond study areas.

Classification and case definition

The 1985 WHO classification of diabetes and diagnostic criteria (18) are the basis of the minimum set of criteria for the WHO DiaMond incidence study. Eligible individuals were placed on daily insulin injections before their 15th birthdays and were residents in the area of registration at the time of the first insulin administration.

A total of 100 centers from 50 countries are participating in the WHO Dia-Mond incidence study and are submitting incidence data on type 1 diabetes. Of these centers, 25 are taking part in the WHO DiaMond project through the EURODIAB Aetiology of Childhood Diabetes on an Epidemiological Basis (ACE) Study (3). Registries are either prospective, retrospective, or a combination of both. Participating centers have submitted annual incidence data to the WHO DiaMond data center in Helsinki using standardized forms. Data on sex, ethnic group, date of birth, date of first insulin administration, source of data on family history of diabetes (the diabetes status of siblings, parents, and children of registered cases) are included in the database. Additional registries are participating in the WHO DiaMond project and began data collection after the year 1994 and therefore are not included in this article.

Quality control of data

Each data file analyzed in the data center was sent back to the centers for final checking and data cleaning to ensure the accuracy of the data. Completeness of registration was confirmed by estimating the degree of ascertainment using the capture-recapture method (19) in most centers. In some centers, this was not necessary because of complete coverage of the primary source. According to the WHO DiaMond methods of operation, the primary data source consists of the cases of type 1 diabetes who fulfill the criteria for registration and have been identified from hospital records or from the records of pediatricians or family physicians. As a secondary (independent) source for cases, records of the local diabetes association, school health records, or social insurance schemes have been used.

Statistical methods

Incidence rates were calculated as the incidence per calendar year and 100,000 individuals at risk. Age adjustment for the rates was done in 5-year intervals (0-4, 5-9, and 10-14 years) using the direct method with a standard population consisting of equal numbers of children in each of 3 subgroups. The 95% CIs were estimated assuming the Poisson distribution of the cases. The distribution of incidence rates was arbitrarily divided into five groups: 1) very low, <1/100,000 per year; 2) low, 1-4.99/100,000 per year; 3) intermediate, 5-9.99/100,000 per year; high, 4) 10-19.99/100,000 per year; and 5) very high, \geq 20/100,000 per year.

RESULTS— The overall age-adjusted incidence rates of type 1 diabetes varied from 0.1/100,000 per year in Zunyi, China, and Caracas, Venezuela, to 36.8/100,000 per year in Sardinia and 36.5/100,000 per year in Finland. This represents a >350-fold variation in the incidence among the 100 populations worldwide (Table 1). One-third of the populations (33 of 100) had an intermediate incidence of type 1 diabetes. The variation in incidence is described also in Fig. 1, where the incidence of different participating centers in 50 countries is arranged in descending order according to the incidence.

The populations on the African continent (all from northern Africa) had intermediate incidence rates of type 1 diabetes. Only Mauritius, the island on the east coast of the continent, had a low incidence. Most of the populations in the Asian continent (27 of 29) had a very low or low incidence. Exceptions were Israel with an intermediate incidence and Kuwait with a high incidence, both of which represent Caucasoid populations. Of the European populations, one-half (18 of 39) had intermediate incidence rates, and the rest (21 of 39) had high or very high incidence rates. Particularly high incidence rates occurred in Sardinia and Finland $(\sim 37/100,000 \text{ per year})$. Other populations with very high incidence rates in Europe were in Sweden and Norway. Despite the small total number of cases in Portalegre, Portugal, the incidence of type 1 diabetes was consistently high each year during the study. Among all North American populations, incidence rates were high. In Canada, Alberta and Prince Edward Island had particularly high incidence rates. The incidence of type 1 diabetes among populations in South America ranged from intermediate (5 of 11) to very low (3 of 11). In Central

Table 1—Age-standardized incidence of type 1 diabetes in children ≤14 years of age (per 100,000 per year)

	C. 1	T		Ţ,	ncidence		Cases		
Region (country and area)	Study period	Estimate of ascertainment (%)	Boys Girls		Total (95% CI)	Boys:girls	Boys	Girls	Total
Africa	<u> </u>	. ,		-		7 0			
Alica									
Oran*	1990		4.4	7.0	5.7 (3.62-8.52)	0.6	9	14	23
Tunisia	1990		4.4	7.0	3.7 (3.02-0.32)	0.0	9	14	23
Beja*	1990-1994		9.0	6.5	7.8 (5.47–10.68)	1.2	22	16	38
Gafsa*	1990-1994		10.0	7.5	8.8 (6.59–11.51)	1.2	31	22	53
Kairoan*	1991-1993		5.5	5.9	5.7 (3.95–7.89)	0.9	23	23	46
Monastir*	1990–1994		4.7	5.2	4.9 (3.35–6.96)	0.8	15	16	31
Sudan	1000 1004		3.1	5.2	4.0 (0.00-0.00)	0.0	13	10	31
Gezira	1990	100	5.6	4.4	5.0 (3.74-6.54)	1.3	17	12	29
Mauritius	1990–1994	35–100	1.3	1.5	1.4 (0.83–2.07)	0.9	10	11	21
Asia	1000 1001	00 100	1.0	1.0	1.1 (0.00-2.01)	0.5	10	11	21
China									
Wuhan	1990-1994	100	5.2	3.8	4.6 (2.81-6.96)	1.4	13	9	22
Sichuan	1990-1994	80-100	1.8	2.7	2.3 (1.45–3.34)	0.7	9	13	22
Huhehot	1990-1994	100	1.1	0.7	0.9 (0.54–1.53)	1.6	10	6	16
Dalian	1990-1994	100	1.1	1.2	1.2 (0.75–1.76)	0.9	10	11	21
Guilin	1991-1994	100	0.6	1.0	0.8 (0.22-2.01)	0.6	2	3	5
Beijing*	1990-1994		0.7	1.1	0.9 (0.72–1.09)	0.6	38	52	90
Shanghai	1990-1994	69-100	0.7	0.7	0.7 (0.51-0.91)	1.0	24	23	47
Chang Chun	1990-1994	86-100	0.6	1.1	0.8 (0.49-1.30)	0.5	7	11	18
Nanjing	1990-1994	100	0.6	1.1	0.8 (0.51-1.29)	0.5	7	13	20
Jinan	1990-1994	100	0.4	0.4	0.4 (0.25-0.59)	1.0	12	11	23
Jilin	1990-1994	100	0.4	0.8	0.6 (0.38-0.90)	0.5	8	14	22
Shenyang	1990-1994	100	0.4	0.5	0.5 (0.29-0.67)	0.8	12	13	25
Lanzhou	1991-1994	100	0.5	0.3	0.4 (0.15-0.68)	1.7	5	3	8
Harbin	1990-1994	100	0.3	0.3	0.3 (0.19-0.38)	1.0	18	17	35
Nanning	1990-1994	100	0.3	0.7	0.5 (0.25-0.78)	0.4	4	10	14
Changsha	1990-1994	100	0.3	0.2	0.3 (0.16-0.42)	1.5	10	7	17
Zhengzhou	1991–1994	86-100	0.2	1.0	0.6 (0.30-1.10)	0.2	2	8	10
Hainan	1990–1994	100	0.1	0.2	0.2 (0.09-0.25)	0.5	6	11	17
Tie Ling	1990–1994	100	0.2	0.2	0.2 (0.13-0.26)	1.0	5	3	8
Zunyi	1990–1992	100	0.1	0.1	0.1 (0.00-0.37)	1.0	1	2	3
Wulumuqi	1990-1994	100	0.9	8.0	0.8 (0.34–1.71)	1.1	5	4	9
Hong Kong*	1990-1994		0.6	2.1	1.3 (0.77–2.17)	0.3	4	13	17
Kuwait	1992–1994	91–100	19.2	17.3	18.3 (15.52–21.35)	1.1	82	71	153
Israel†	1990–1994	100	5.5	6.6	6.0 (5.42–6.67)	0.8	167	194	361
Japan	1000 1000			1.0	1 4 (1 07 1 01)	0.0	0.7	0.4	24
Chiba*	1990–1993	100	1.2	1.6	1.4 (1.07–1.81)	0.8	27	34	61
Hokkaido	1990–1993	100	2.2	2.1	2.2 (1.71–2.65)	1.0	45	44	89
Okinawa	1990–1993	77–100	1.0	1.8	1.4 (0.81-2.24)	0.6	6	11	17
Pakistan Karachi	1990	51	0.5	0.9	0.7 (0.44-0.99)	0.6	0	16	25
Russia	1990	31	0.5	0.9	0.7 (0.44-0.99)	0.6	9	16	25
Novosibirsk	1990-1994	87–100	5.7	6.4	6.0 (5.18-6.94)	0.9	90	101	101
Europe	1990-1994	07-100	3.7	0.4	0.0 (5.16-0.94)	0.9	90	101	191
Austria†	1990-1994	99-100	9.8	9.3	9.6 (8.84–10.31)	1.1	348	312	660
Belgium†	1990-1994	33-100	5.0	3.5	3.0 (0.04-10.31)	1.1	340	312	000
Antwerpen	1990-1994	90-100	10.5	12.8	11.6 (9.40-14.21)	0.9	44	51	95
Bulgaria	1550-1554	30-100	10.5	12.0	11.0 (3.40-14.21)	0.5	44	JI	. 93
Varna	1990-1994	100	5.9	7.6	6.8 (5.80–7.83)	0.8	82	100	182
Varna West Bulgaria	1990-1994	99–100	9.9	10.0	9.9 (8.71–11.21)	1.0	131	125	256
Denmark†	1930-1934	33-100	3.3	10.0	J.J (U.11-11.21)	1.0	131	123	230
4 counties	1990-1994	83-100	16.4	14.5	15.5 (13.28–17.95)	1.1	96	81	177
	1000 1001		+0.7	11.0	10.0 (10.20 17.00)	4.1		01	

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Table 1—Continued

	Study	Estimate of		Ir	ncidence			Cases		
Region (country and area)	period	ascertainment (%)	Boys	Girls	Total (95% CI)	Boys/girls	Boys	Girls	Total	
Estonia*	1990–1994	· · · · · · · · · · · · · · · · · · ·	9.9	11.2	10.5 (9.05–12.20)	0.9	85	93	178	
Finland*	1990-1994		37.0	36.0	36.5 (34.83–38.26)	1.0	915	853	1,768	
Francet					,	-				
4 regions	1990-1994	95-99	8.7	8.3	8.5 (7.86-9.12)	1.0	372	337	709	
Germany†					,					
Baden-Württemberg	1990-1994	91-100	11.0	10.9	11.0 (10.25-11.69)	1.0	463	440	903	
Greece†										
Attica	1990-1994	100	10.2	9.1	9.7 (8.55-10.92)	1.1	149	124	273	
Hungary†										
18 counties	1990–1994	99-100	8.7	9.6	9.1 (8.43–9.81)	0.9	337	360	697	
Italy										
Sardinia†	1990–1994	37-85	43.6	29.5	36.8 (33.72–39.98)	1.5‡	337	211	548	
Eastern Sicily†	1990–1994	96–100	13.4	9.9	11.7 (9.78–13.93)	1.4	75	53	128	
Pavia	1990–1994	100	11.6	11.9	11.7 (8.08–16.44)	1.0	17	17	34	
Marche	1990–1994	100	10.5	8.9	9.7 (7.90–11.84)	1.2	55	44	99	
Turin	1990-1994	97–100	11.9	10.1	11.0 (9.32–12.15)	1.2	86	69	155	
Lazio*†	1990-1994	100	8.0	8.3	8.1 (7.28–9.07)	1.0	164	162	326	
Lombardia†	1990–1994	100	7.6	6.8	7.2 (6.55–7.92)	1.1	239	204	443	
Latvia	1990-1992	100	7.0	5.7	5.9 (5.06–6.98)	1.2	59	47	106	
Lithuania	1990–1994	100	7.7	7.1	7.4 (6.57–8.25)	1.1	162	145	307	
Luxemburg†	1990–1994	100	12.6	10.2	11.4 (8.14–15.59)	1.2	22	17	39	
The Netherlands†	1000 1001	07.00	100	100	10.0 (11.00.14.40)	1.0	170	175	252	
5 regions	1990–1994	87–98	12.9	13.2	13.0 (11.69–14.42)	1.0	178	175	353	
Norway†	1000 1004	01 100	22.4	10.0	01.0 (10.10.00.00)		222	107	400	
8 counties	1990–1994	91–100	22.4	19.9	21.2 (19.18–23.29)	1.1	222	187	409	
Poland Krakow*	1000 1004		6.1	6.1	C 1 /E 20 C 02\	1.0	134	126	260	
	1990–1994 1990	100	4.1	6.0	6.1 (5.38–6.92)	0.7	28	40	68	
Wielkopolska	1990	100	4.1	0.0	5.0 (3.88–6.36)	0.7	20	40	00	
Portugal	1990-1994	74-100	16.3	12.9	14.6 (10.62-19.64)	1.3	26	19	45	
Algarve†	1990-1994	100	9.4	9.9	9.7 (6.76–13.36)	0.9	19	19	38	
Coimbra Madeira Island†	1990-1994	100	6.9	7.5	7.2 (4.46–11.05)	0.9	10	11	21	
	1990-1994	86–100	15.9	26.7	21.1 (13.29–31.89)	0.9	9	14	23	
Portalegre† Romania†	1990-1994	100	13.5	20.1	21.1 (13.23–31.03)	0.0	9	14	23	
Bucharest	1990-1994	100	4.2	5.9	5.0 (4.14-6.05)	0.7	52	65	117	
Slovenia†	1990-1994	100	6.8	9.0	7.9 (6.68–9.23)	0.8	70	88	158	
Slovakia	1990–1994	100	7.9	9.1	8.5 (7.81–9.25)	0.9	261	289	550	
Spain	1330-1334	100	1.5	3.1	0.5 (1.01-5.25)	0.5	201	200	330	
Catalonia	1990-1994	81-100	12.5	12.6	12.5 (11.55-13.50)	1.0	358	338	696	
Sweden*	1990-1994	100	28.1	26.9	27.5 (26.36–28.67)	1.0		1,031	2,166	
U.K.	1550-1554	100	20.1	20.0	27.0 (20.00 20.01)	1.0	1,100	1,001	2,100	
Aberdeen	1990	51	32.5	15.0	24.0 (15.22–36.01)	2.2	16	7	23	
Leicestershire†	1990-1994	97–100	15.4	15.3	15.3 (12.85–18.07)	1.0	70	66	136	
Northern Ireland†	1990-1994	95–100	20.1	19.3	19.7 (17.81-21.79)	1.0	202	185	387	
Oxford*†	1990–1994	00 100	20.1	15.3	17.8 (16.18–19.46)	1.3‡	266	191	457	
Plymouth	1990-1994	96-100	16.5	18.1	17.3 (14.41–20.53)	0.9	63	65	128	
North America	1000 1001	00 100	10.0	10.1	17.0 (11.11 20.00)	0.0	•	•	100	
Canada										
Alberta	1990-1994	75–96	23.4	24.7	24.0 (20.62-27.82)	0.9	87	88	175	
Prince Edward Island*	1990–1993	100	28.0	20.8	24.5 (16.38–35.16)	1.3	17	12	29	
U.S.					()					
Allegheny, PA	1990-1994	87-100	19.1	16.4	17.8 (15.45-20.33)	1.2	112	94	206	
Jefferson, AL*	1990-1994	-: 	14.6	15.4	15.0 (12.21–18.22)	0.9	50	51	101	
Chicago, IL§	1990-1994	51-100	10.2	13.3	11.7 (10.47–13.12)	0.8	131	169	300	
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Table 1-Continued

	Study	Estimate of		Ir	ncidence		Cases		
Region (country and area)	period	ascertainment (%)	Boys	Girls	Total (95% CI)	Boys/girls	Boys	Girls	Total
South America									
Argentina									
Avellaneda	1990-1994	88-97	5.6	7.5	6.5 (4.31-9.51)	0.7	11	15	26
Cordoba	1991–1992	88-92	6.2	7.9	7.0 (5.20–9.26)	0.8	21	26	47
Corrientes	1992-1994	90–100	2.9	5.7	4.3 (2.21–7.51)	0.5	4	8	12
Tierra del Fuego	1993-1994	100	20.2	0	8.0 (2.18–17.60)		4	0	4
Brazil				•	0.0 (2.10 100)	•	-	•	-
Sao Paulo	1990-1992	70–95	6.9	9.1	8.0 (5.53-11.14)	0.8	15	19	34
Chile	1000 100.		0.0	0.1	0.0 (0.00 11.11)	0.0			0.1
Santiago	1990-1992	100	1.7	1.5	1.6 (1.28-2.04)	1.1	66	56	122
Colombia					310 (3130 2131)				
Santafe de Bogota	1990	97	4.7	2.9	3.8 (2.88-4.93)	1.6‡	35	21	56
Paraguay*	1990–1994	•	1.0	0.8	0.9 (0.71–1.11)	1.3	45	34	79
Peru									
Lima	1990-1991	88	0.2	0.6	0.4 (0.22-0.61)	0.3	4	12	16
Uruguay					(,				
Montevideo	1992	97	8.3	8.3	8.3 (5.38-12.10)	1.0	13	13	26
Venezuela					,				
Caracas (second center)*	1992		0.1	0.2	0.1 (0.09-0.18)	0.5	18	25	43
Central America and West Indies					, ,				
Barbados*	1990-1993		2.4	1.6	2.0 (0.32-6.36)	1.5	3	2	5
Cuba	1990-1994	75-100	2.5	3.4	2.9 (2.63-3.24)	0.7	152	197	349
Dominica	1990-1993		6.6	4.9	5.7 (1.53-14.65)	1.5	3	2	5
Mexico					·				
Veracruz	1990-1993	100			1.5 (0.70-2.94)		3	6	9
Puerto Rico (U.S.)	1990-1994	90-97	16.2	18.7	17.4 (16.25-18.63)	0.9	398	445	844
Virgin Islands (U.S.)*	1990-1994		14.7	11.5	13.1 (7.64-21.01)	1.4	9	7	16
Oceania									
Australia									
New South Wales	1990-1993	89-100	13.1	15.9	14.5 (13.42-15.55)	0.8	335	387	722
New Zealand									
Auckland	1990-1994	100	12.3	13.6	12.9 (10.87-15.28)	0.9	65	70	135
Canterbury	1990-1994	100	23.9	19.8	21.9 (17.33-27.32)	1.2	43	35	78
Data am incidence rates or incidence	(050/ CD		*D_:		The TELIPODIAR ACE St.			C A E - :	Α

Data are incidence rates or incidence rates (95% CI) unless otherwise indicated. *Primary source only; †EURODIAB ACE Study; ‡statistically significant; §African-American and Hispanic.

America and the West Indies, the populations in Puerto Rico and Virgin Islands had high incidence rates, and the rest of the populations had intermediate or low incidence rates. In Oceania, the incidence rates were high in Australia and New Zealand, particularly in the Canterbury region of New Zealand.

Noticeable within-country variation in incidence rates was observed in Italy, where the incidence in Sardinia (36.8/100,000 per year) was 3–5 times higher than the incidence rates in the centers in continental Italy. In Portugal, the difference in incidence rates between centers was 3-fold and was lowest on Madeira Island (7.2/100,000 per year) and highest in Portalegre (21.1/100,000 per year); however, the number of cases in all Portugese centers

was relatively small. In New Zealand, the incidence in Canterbury was 21.9/100,000 per year and was only half of that in Auckland (12.3/100,000 per year). Nearly 50-fold within-country variation was observed in China, where incidence rates varied from 0.1/100,000 per year in Zunyi to 4.6/100,000 per year in Wuhan. In some Chinese centers, the total number of cases was small; therefore, the results should be interpreted with caution.

The male-to-female ratio in incidence was calculated for 98 populations (Table 1). A statistically significant male excess in incidence rate was found in Sardinia (Italy), Oxford (U.K.), and Santafe de Bogota (Columbia). No populations had a statistically significant female excess in incidence rate.

Age-specific incidence of type 1 diabetes was calculated in 5-year age-groups (0–4, 5–9, and 10–14 years) (Table 2). In most populations, the incidence rates increased with age and were the highest among children 10–14 years of age. The variation in incidence rates across age-groups was examined using pooled population and incidence data from all centers in the linear regression model. The difference in incidence rates between the age-groups was statistically significant (P < 0.0001). However, in some populations, the incidence rates were nearly the same in all 3 age-groups.

conclusions— The sample population (75.1 million) for which the incidence of type 1 diabetes is estimated covers

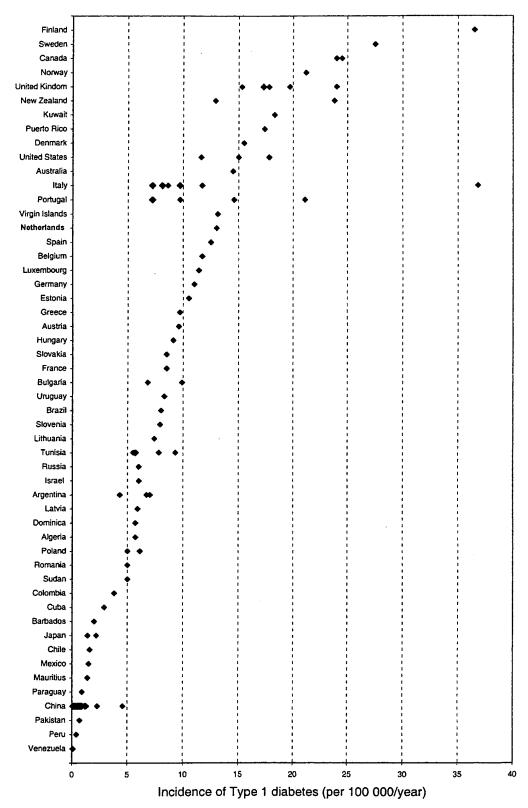


Figure 1—Age-standardized incidence (per 100,000 per year) of type 1 diabetes in children ≤ 14 years of age in 100 populations. Data for boys and girls have been pooled. Countries are arranged in descending order according to the incidence. (Puerto Rico and Virgin Islands are presented separately from other populations in the U.S.)

Table 2—Age-specific incidence of type 1 diabetes in children \leq 14 years of age (per 100,000 per year)

		Boys			Girls		Total			
Region (country and area)	0-4 years		10-14 years	0-4 years	5-9 years	10-14 years	0-4 years	5-9 years	10-14 years	
Africa				W. W			· · · · · · · · · · · · · · · · · · ·			
Algeria										
Oran*	2.8	4.3	6.1	5.8	5.8	9.4	4.3	5.0	7.8	
Tunisia	2.0	1.0		3.0	3.0	3.4	4.5	3.0	7.0	
Beja*	11.0	6.1	10.0	1.4	6.4	11.6	6.3	6.2	10.8	
Gafsa*	3.1	9.6	17.3	2.2	6.0	14.3	2.7	7.8	15.8	
Kairoan*	6.4	4.7	10.9	1.0	9.1	13.5	3.8	6.8	12.1	
Monastir*	1.9	3.6	8.5	2.9						
	1.9	3.0	8.5	2.9	1.8	11.0	2.3	2.7	9.7	
Sudan	1.0	2.7	11.0	0.0		10.4	0.0	0.0	11.0	
Gezira	1.2	3.7	11.9	0.6	2.1	10.4	0.9	2.9	11.2	
Mauritius	0.8	0.4	2.5	0.8	1.3	2.2	8.0	0.9	2.4	
Asia										
China										
Wuhan	3.6	6.8	5.3	2.0	3.6	5.8	2.8	5.2	5.6	
Sichuan	0.5	0.5	4.5	0.5	2.3	5.3	0.5	1.4	4.9	
Huhehot	0.0	1.9	1.5	0.4	1.1	0.8	0.2	1.5	1.2	
· Dalian	0.5	0.9	2.1	1.0	0.9	1.8	0.7	0.9	1.9	
Guilin	0.0	0.0	1.9	0.0	1.0	2.0	0.0	0.5	1.9	
Beijing*	0.4	0.7	1.0	0.3	1.0	2.1	0.4	8.0	1.5	
Shanghai	0.7	0.7	0.6	0.4	8.0	0.9	0.5	0.8	0.8	
Chang Chun	1.1	0.3	0.6	0.3	1.1	1.8	0.7	0.7	1.1	
Nanjing	0.2	0.5	1.0	1.3	1.0	1.1	0.7	0.7	1.0	
Jinan	0.1	0.2	0.9	0.2	0.6	0.4	0.1	0.4	0.7	
Jilin	0.5	0.5	0.3	0.2	0.5	1.7	0.3	0.5	1.0	
Shenyang	0.2	0.4	0.7	0.2	0.6	0.6	0.2	0.5	0.6	
Lanzhou	0.0	0.5	0.8	0.4	0.3	0.0	0.2	0.4	0.4	
Harbin	0.2	0.3	0.3	0.0	0.3	0.5	0.1	0.3	0.4	
Nanning	0.0	0.2	0.6	0.2	1.2	0.6	0.1	0.7	0.4	
Changsha	0.2	0.2	0.5	0.1	0.0	0.6	0.1	0.1	0.6	
Zhengzhou	0.3	0.4	0.0	0.3	0.8	2.0	0.2	0.1	1.0	
Hainan	0.00	0.4	0.28	0.06	0.8	0.38	0.03	0.0	0.33	
Tie Ling	0.13	0.30	0.25		0.21					
	0.13	0.30		0.00		0.13 0.28	0.07	0.31	0.19	
Zunyi	0.00		0.00	0.00	0.00		0.00	0.09	0.13	
Wulumuqi		0.6	2.1	0.5	0.6	. 1.1	0.3	0.6	1.6	
Hong Kong*	0.5	0.5	0.9	0.0	3.0	3.4	0.3	1.7	2.1	
Kuwait	16.2	17.0	24.4	10.0	18.6	23.3	13.2	17.8	23.8	
Israel†	2.4	5.6	8.4	2.5	7.8	9.5	2.5	6.7	8.9	
Japan										
Chiba*	0.8	0.7	2.0	1.2	1.6	2.0	1.0	1.2	2.0	
Hokkaido	1.9	1.5	3.1	0.6	2.3	3.5	1.3	1.9	3.3	
Okinawa	1.6	0.0	1.4	0.6	1.0	3.9	1.1	0.5	2.6	
Pakistan										
Karachi	0.2	0.9	0.3	0.5	0.3	2.0	0.3	0.6	1.1	
Russia										
Novosibirsk	5.8	5.5	5.8	2.8	8.0	8.3	4.3	6.7	7.0	
Europe										
Austria†	5.9	11.4	12.1	4.7	9.8	13.3	5.3	10.6	12.7	
Belgium†										
Antwerpen	6.3	10.2	15.3	6.6	12.9	19.1	6.4	11.5	17.2	
Bulgaria		-	-	- : -		-	· -		- · · -	
Varna	3.3	5.5	9.0	4.4	7.7	10.8	3.8	6.6	9.9	
West Bulgaria	5.9	10.6	13.0	7.3	9.0	13.5	6.6	9.8	13.3	
Denmark†	2.0	20.0	10.0	, .5	0.0	10.0	5.5	0.0	10.0	
4 counties	8.6	16.5	24.2	6.4	14.9	22.2	7.5	15.7	23.3	
	5.0	10.0	L 1. L	U. 1	17.0	44.6	7.0	10.1	20.0	

(continued on page 1523)

Table 2—Continued

Region (country and area) 0-4 years 5-9 years 10-14 years 5-9 years 10-14 years 5-9 years 6-9 years 6-9 years 16.4 7.4 9.7 16.4 7.8 8.9 8.9 10.5 11.6 4.8 8.7 11.4 4.7 9.3 9.3 9.3 11.4 4.7 9.3 9.3 9.3 11.1 11.6 11.6 11.6 11.6	10-14 years 14.9 39.6 11.5 14.7 13.3 11.9
Finland* 28.5 40.6 41.8 30.7 40.3 37.1 29.6 40.5 France† 4 regions 4.6 9.9 11.6 4.8 8.7 11.4 4.7 9.3 Germany† Baden-Württemberg 6.7 10.5 15.8 7.6 11.6 13.5 7.1 11.1 Greece†	39.6 11.5 14.7 13.3
Finland* 28.5 40.6 41.8 30.7 40.3 37.1 29.6 40.5 France† 4 regions 4.6 9.9 11.6 4.8 8.7 11.4 4.7 9.3 Germany† Baden-Württemberg 6.7 10.5 15.8 7.6 11.6 13.5 7.1 11.1 Greece†	39.6 11.5 14.7 13.3
France† 4 regions 4.6 9.9 11.6 4.8 8.7 11.4 4.7 9.3 Germany† Baden-Württemberg 6.7 10.5 15.8 7.6 11.6 13.5 7.1 11.1 Greece†	14.7 13.3
Germany† Baden-Württemberg 6.7 10.5 15.8 7.6 11.6 13.5 7.1 11.1 Greece†	14.7 13.3
Baden-Württemberg 6.7 10.5 15.8 7.6 11.6 13.5 7.1 11.1 Greece†	13.3
Greece†	13.3
·	
Attica 6.6 8.3 15.7 7.0 9.6 10.8 6.8 8.9	11.9
Hungary†	11.9
18 counties 5.7 9.2 11.1 5.8 10.1 12.8 5.8 9.6	
Italy	
Sardinia† 32.6 48.3 49.9 25.7 34.1 28.6 29.2 41.4	39.6
Eastern Sicily† 10.5 18.1 11.6 7.7 11.1 11.1 9.1 14.7	11.3
Pavia 8.8 13.1 12.8 2.3 13.9 19.4 5.7 13.5	16.0
Marche 7.7 13.2 10.6 4.8 13.3 8.6 6.3 13.3	9.6
Turin 9.3 12.2 14.0 9.8 8.8 11.7 9.5 10.5	12.9
Lazio*† 6.5 9.0 8.4 6.7 9.8 8.4 6.6 9.4	8.4
Lombardia† 6.6 7.9 8.4 5.1 7.0 8.3 5.9 7.5	8.3
Latvia 3.3 5.6 12.0 3.1 4.8 9.3 3.2 5.2	10.7
Lithuania 4.7 8.0 10.3 3.1 8.7 9.4 3.9 8.3	9.9
Luxemburg† 9.5 10.4 18.0 8.3 11.0 11.3 8.9 10.7	14.7
The Netherlands†	
5 regions 9.3 12.3 17.1 9.7 15.0 14.8 9.5 13.6	15.9
Norway†	
8 counties 14.3 23.0 29.8 10.1 20.9 28.6 12.3 22.0	29.2
Poland	
Krakow* 3.0 5.7 9.6 3.5 7.3 7.5 3.2 6.5	8.6
Wielkopolska 2.9 4.2 5.2 2.0 6.9 9.0 2.5 5.5	7.1
Portugal	
Algarve† 12.8 8.1 28.0 11.1 15.0 12.6 12.0 11.4	20.5
Coimbra 3.8 11.4 13.1 2.0 15.5 12.2 2.9 13.4	12.7
Madeira Island† 9.1 6.1 5.5 7.1 2.2 13.2 8.1 4.2	9.3
Portalegre† 5.1 27.7 19.3 11.2 44.8 30.4 8.0 35.9	24.8
Romania†	
Bucharest 0.9 4.3 7.5 3.6 9.7 4.4 2.2 6.9	6.0
Slovenia† 5.6 5.1 9.8 6.3 8.8 12.0 5.9 6.9	10.9
Slovakia 6.3 7.3 10.1 6.5 9.7 11.2 6.4 8.5	10.6
Spain 50 100 100 100 105 100 100 100 100 100	10.0
Catalonia 5.6 12.8 18.9 5.0 13.5 19.2 5.3 13.1	19.0
Sweden* 19.6 28.9 35.7 17.4 31.8 31.5 18.5 30.3	33.7.
U.K.	25.0
Aberdeen 24.1 30.4 43.0 12.6 25.8 6.5 18.5 28.2	25.3
Leicestershire† 6.2 16.8 23.1 10.6 15.0 20.1 8.4 15.9	21.7
Northern Ireland† 11.4 22.4 26.6 10.4 22.4 25.1 10.9 22.4	25.9
Oxford*† 15.6 19.0 25.6 12.4 12.5 21.1 14.0 15.8	23.5
Plymouth 15.5 16.5 17.6 12.2 19.3 22.7 13.9 17.9	20.1
North America	
Canada	
Alberta 9.0 26.0 35.2 19.1 24.4 30.7 13.9 25.2	33.0
Prince Edward Island* 15.0 34.6 34.4 10.5 25.8 26.1 12.8 30.3	30.3
U.S.	
Allegheny, PA 7.4 19.4 30.4 10.1 19.2 20.0 8.7 19.3	25.3
Jefferson, AL* 9.7 13.8 20.3 6.5 15.1 24.6 8.1 14.4	22.4
Chicago, IL‡ 4.4 9.1 16.9 5.0 12.4 22.6 4.7 10.7	19.8

(continued on page 1524)

Worldwide type 1 diabetes incidence

Table 2—Continued

Region (country and area)	Boys				Girls		Total		
	0-4 years	5-9 years	10-14 years	0-4 years	5-9 years	10-14 years	0-4 years	5-9 years	10-14 years
South America									
Argentina									
Avellaneda	2.1	2.4	8.3	0.0	24.7	2.8	1.1	13.4	5.6
Cordoba	3.6	6.0	9.0	2.2	11.4	10.0	2.9	8.7	9.5
Corrientes	3.9	0.0	4.7	6.0	6.7	4.6	5.0	3.3	4.6
Tierra del Fuego	0	0	60.6	0	0	0	0	0	30.3
Brazil									
Sao Paulo	4.1	6.9	9.8	5.6	8.5	13.0	4.8	7.7	11.4
Chile									
Santiago	1.5	3.1	4.1	1.4	1.3	5.0	1.5	2.2	4.6
Colombia									
Santafe de Bogota	3.0	3.9	7.3	2.0	2.8	3.9	2.5	3.3	5.6
Paraguay*	0.7	0.6	1.8	0.5	1.0	0.8	0.6	0.8	1.3
Peru									
Lima	0.1	0.0	0.4	0.4	0.7	0.6	0.3	0.4	0.5
Uruguay									
Montevideo	0.0	3.6	21.2	2.0	14.8	7.9	1.0	9.1	14.7
Venezuela									
Caracas (second center)*	0.1	0.2	0.0	0.1	0.2	0.2	0.1	0.2	0.1
Central America and West Indies									
Barbados*	2.5	4.7	0.0	0.0	2.3	2.3	1.3	3.5	1.2
Cuba	1.1	2.9	3.5	1.9	3.8	4.5	1.5	3.3	4.0
Dominica	0.0	8.2	13.5	0.0	0.0	. 14.6	0.0	4.0	14.1
Mexico									
Veracruz							0.5	2.0	2.1
Puerto Rico (U.S.)	12.1	16.6	19.8	9.8	21.9	24.2	11.0	19.2	22.0
Virgin Islands (U.S.)*	15.9	14.3	13.9	10.8	9.7	14.1	13.4	12.0	14.0
Oceania									
Australia									
New South Wales	8.1	12.3	18.9	10.1	16.8	20.8	9.1	14.5	19.8
New Zealand									
Auckland	4.5	18.7	13.8	8.8	14.0	17.9	6.6	16.4	15.8
Canterbury	12.6	31.2	28.0	19.6	15.9	24.0	16.0	23.7	26.1

Data are incidence rates. *Primary source only; †EURODIAB ACE Study; ‡African-American and Hispanic.

4.5% of the world's population ≤ 14 years of age. To our knowledge, this represents the largest standardized survey for any disease. Most of the incidence data come from European countries. During the first half of the 1990s, several incidence registries were established in the Asian continent — most of them in China. Although incidence data from North and South America and Africa are still sparse, the increased information on the incidence of type 1 diabetes among Asian populations has changed the pattern of global variation in incidence. The difference between the highest incidence rates in Sardinia and Finland and the lowest incidence rate in China was >350-fold during the first half of the 1990s.

The incidence of type 1 diabetes appears to be increasing in almost all pop-

ulations worldwide, and the increase is particularly high in populations with a low incidence (20). Whether this is a true increase resulting from changing environmental or lifestyle factors or is simply an improvement in case ascertainment is currently impossible to determine because the 5-year period covered in this analysis is too short to accumulate enough cases for appropriate analysis. Also, the within-country variation in incidence in some countries may be random because of a small number of cases; therefore, data for a longer period are needed before those spatial differences could be confirmed.

The WHO DiaMond project (21) is a global effort to determine for the first time the incidence of type 1 diabetes using standardized incidence registries where the

degree of ascertainment is based on the capture-recapture method to determine the degree of underestimation of cases (19). An underestimation is probably inherent in all registration systems, but the problem can be avoided by using statistical methods to measure and adjust for it. In practice, in some countries collecting incidence data on type 1 diabetes, secondary sources for ascertainment of cases are not available or are difficult to find. However. 80% of registries checked for underestimation used 2 independent sources and the capture-recapture method (19). Two populations had very low case ascertainment rates (50%); however, data from these populations were available only for 1 year, so the results should be interpreted with caution.

The global pattern of the incidence of type 1 diabetes has not changed markedly since the reports published during the 1970s and 1980s. The earlier assumed polar-equatorial gradient in the incidence of type 1 diabetes (1,2,4,5) does not seem to be as strong as previously assumed. From 1990 to 1994, the incidence rates of type 1 diabetes were highest in Sardinia and Finland. However, these populations are 3,000 km from each other and have different environments and distinctive genetic backgrounds (22,23). The incidence rates in these populations were substantially higher than those in the other high-incidence populations presented in this report. Although the populations with very high incidence rates were europid populations in Europe and other continents, populations with a relatively high incidence rate were also found in tropical or subtropical areas such as Kuwait (24) and Puerto Rico (25). In fact, a relatively wide gradient of risk was observed among some noneuropid ethnic groups (i.e., admixed partly African [1.4/100,000 per year in Mauritius vs. 15.0/ 100,000 per year in Chicago] and Arab [5.0/100,000 per year in Sudan vs. 18.3/ 100,000 per year in Kuwait] populations). The explanation for these wide risk disparities within ethnic groups may lie in differences in genetic admixture or environmental/ behavioral factors. Although this study provides the most comprehensive data on the incidence of childhood diabetes and its variation worldwide, it cannot give answers about the reasons behind such a huge between-population variation. Such descriptive data are, however, necessary for the development and testing of potential genetic and environmental hypotheses. One of the aims in establishing the epidemiological databases within the WHO DiaMond project was to create opportunities for further research into etiological factors in type 1 diabetes. These population-based studies have already generated a large number of etiological studies. Certainly, in those societies undergoing rapid social change, population levels of exposure to presumed etiological agents for type 1 diabetes change rapidly during a relatively short period of time. Clearly, continuing and expanding surveillance for childhood diabetes across the world represents one of the most potent strategies for understanding the multifactorial etiology of the disease and ultimately preventing it.

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APPENIX

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